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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,507	12/22/2004	Igor Stagljar	3032-101	6720

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EXAMINER	
JOIKE, MICHELE K	

ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,507	STAGLJAR ET AL.	
	Examiner	Art Unit	
	Michele K. Joike	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *48-81* is/are pending in the application.

4a) Of the above claim(s) *69* is/are withdrawn from consideration.

5)☒ Claim(s) *74* is/are allowed.

6)☒ Claim(s) *48-68, 70-73, 75-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 48-81 are pending in the instant application. Claim 69 is withdrawn; claims 48-68 and 70-81 are examined. Any rejection of record in the previous Office Action, mailed November 17, 2009 that is not addressed in this action has been withdrawn. Because this Office Action introduces new rejections other than those set forth in the previous Office Action, and are not necessitated by amendment, this Office Action is Non-Final.

Claim Objections

Claim 57 stands objected to because of the following informalities: "plamid" should be "plasmid" in lines 7 and 13. Appropriate correction is required.

Response to Arguments Concerning Claim Rejections – 35 USC § 102(b)

Applicant's arguments filed January 19, 2010 have been fully considered and are found to be persuasive.

The following grounds of traversal are presented:

Applicants argue that the bait and prey vectors are maintained episomally. In contrast, Stagljar's bait vector is integrated into the yeast genome. The term "maintained episomally" is consistently used as the opposite of "integrated" in patents covering analogous art including the Examiner's own art unit. Additionally, the claims have been amended to indicate that the vectors are plasmid constructs. Plasmids replicate autonomously. This clarifies that the bait and prey vectors are integrated.

Applicants' arguments (especially pages 9-10) are found to be persuasive for the following reasons. Although the Examiner maintains that "episomal" means "a genetic determinant (as the DNA of some bacteriophages) that can replicate autonomously in bacterial cytoplasm or as an integral part of the chromosomes", the phrase "episomal maintenance" as a term of art means that the DNA is not integrated. Therefore, the 102(b) rejection has been withdrawn; however, a new 35 U.S.C. 103(a) rejection is made.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 48-55, 57-62 and 64-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stagljar in view of US 6,251,676 and US 2005/0277116.

Stagljar et al teaches a split-ubiquitin system for detecting the interaction between two membrane bound proteins by introducing and coexpressing plasmids that encode the fusion proteins Ost-1-Nub or Nub-Alg5 with Wbp1-Cub-PLV into *S. cerevisiae* strain yeast cells carrying *lac*Z and HIS3 reporter genes under the control of LexA-binding sites and testing cells for β-gal activity. The Ost1-Nub fusion protein consists of a portion of Ost1p ER membrane protein and the Nub module. The Nub-Alg5 fusion protein consists of the Alg5 ER membrane protein and the Nub module. The Wbp1-Cub-PLV protein consists of a portion of the Wbp1p ER transmembrane protein, the Cub module, and the PLV transcriptional activator (abstract, page 5187, right column, last paragraph to end of page 5189 and Figure 2). Stagljar et al teach all the features of claims 57-65 in combination, thereby anticipating the kit. Stagljar et al also teach the CEN/ARS, which is a low copy vector present in only 1-2 copies per cell. Stagljar et al teaches all of the limitations as previously described. Regarding claims 66 and 67, Stagljar et al teach a vector (pRS305(Δwbp1-Cub-PLV)) which contains a lacZ selection marker, an E. coli ori, a LEU2 marker, a yeast ori, a T7 promoter, a partial wbp1 sequence, a Cub, and a PLV (as partially evidenced by http://seq.yestgenome.org/vectordb/vector_descrip/COMPLETE/PRS305.SEQ.html). This vector is transformed into a host cell. Therefore, Stagljar et al meet the limitations of claims 66 and 67, as well. However, they do not teach episomal maintenance of the bait and prey vectors.

US 2005/0277116 (paragraph25) teaches that both the bait and prey vectors can be maintained episomally.

US 6,251,676 (column 1) teach a method for protein-protein interaction with bait and prey vectors, wherein the prey vector can be maintained episomally.

The ordinary skilled artisan, desiring to perform a method of identifying compounds for their ability to interfere with protein-protein interaction, would have been motivated to combine the teachings of Stagjlar et al teaching a split-ubiquitin system for detecting the interaction between two membrane bound proteins, as described above, with the teachings of US 2005/ 0277116 and US 6,251,676 because US 6,251,676 teaches that if a plasmid is maintained episomally in a closed circular form, the plasmid can be readily introduced and recovered from a bacterial host cell. It would have been obvious to one of ordinary skill in the art because US 6,251,676 teaches that a vector maintained episomally will not integrate and potentially damage the cell. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 68 and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stagljar et al, US 2005/0277116 and US 6,251,676 as applied to claims 48-55, 57-62 and 64-67 above, and further in view of Ehrhard et al.

Applicants claim a method of identifying compounds for their ability to interfere with protein-protein interaction, using the kit. The compound is a pharmaceutical drug.

Stagljar et al, US 2005/0277116 and US 6,251,676 teach all of the limitations as described above. However, they do not teach identifying a pharmaceutical drug.

Ehrhard et al (Nature Biotch. 18: 1075-1079, 2000, specifically pp. 1075 and 1078) teach a method of identifying compounds for their ability to interfere with protein-protein interaction. One of the proteins is a membrane-bound protein, and the other is soluble. Cells were plated and exposed to different amounts of synthetic α-factor to determine the effect on protein-protein interaction. Since the disclosure does not define pharmaceutical drug, synthetic α-factor is interpreted to be a pharmaceutical drug.

The ordinary skilled artisan, desiring to perform a method of identifying compounds for their ability to interfere with protein-protein interaction, would have been motivated to combine the teachings of Stagjlar et al , US 2005/0277116 and US 6,251,676, as described above, with the teachings of Ehrhard et al, teaching a method of identifying compounds for their ability to interfere with protein-protein interaction because the control of protein-protein interactions is a fundamental aspect of cell regulation. It would have been obvious to one of ordinary skill in the art to perform a method of identifying drugs for their ability to interfere with protein-protein interaction because Ehrhard et al teach this method could be used to identify new inhibitors that could lead to new drugs for the treatment of human disease. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled

artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 56 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stagljar et al, US 2005/0277116 and US 6,251,676 as applied to claims 48-55, 57-62 and 64-67 above, and further in view of Wedegaertner et al and Friedberg et al.

Stagljar et al, US 2005/0277116 and US 6,251,676 teach all of the limitations as described previosuly. However, they do not teach the protein attached artificially to the membrane and the signal sequence encoding a membrane anchor.

Wedegaertner et al (J. Biochem. 270(2): 503-506, 1995, especially p. 503) teach lipid modifications of G proteins so they will attach to the membrane. (Applicants discuss in their specification that fatty acid modification is a means for artificially attaching proteins.)

Friedberg et al (Biochem J. 303: 967-972, 1994) teach an anchor signal sequence attached to a protein.

The ordinary skilled artisan, desiring to artificially attach a protein to the membrane via a membrane anchor, would have been motivated to combine the teachings of Stagjlar et al, US 2005/0277116 and US 6,251,676, as described above, with the teachings of Wedegaertner et al, teaching modifying proteins so they will attach to the membrane with the teachings of Friedberg et al teaching an anchor signal sequence because Friedberg et al teach the attaching a membrane anchor signal sequence to a protein will anchor the protein to the membrane and that heterologous

membrane anchors can be used to transport proteins. It would have been obvious to one of ordinary skill in the art to attach a protein to the membrane because Wedegaertner et al teach that different lipid modifications affect specific protein-protein interactions and localization to specific sites. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 63, 75 and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stagljar et al, US 2005/0277116 and US 6,251,676 as applied to claims 48-55, 57-62, 64-67 above, and further in view of Mumberg et al.

Applicants claims use of a promoter that confers low level expression, wherein the promoter is CYC1.

Stagljar et al, US 2005/0277116 and US 6,251,676 teaches all of the limitations as described above. They teach use of the CUP1 promoter in the pRS314(NubI-ALG5) vector, however, they do not teach the CYC1 promoter.

Mumberg et al (Gene 156: 119-122, 1995) teach use of the CYC1 promoter for expression in yeast.

The ordinary skilled artisan, desiring to use a CYC1 promoter, would have been motivated to combine the teachings of Stagjlar et al, US 2005/0277116 and US 6,251,676, as described above, with the teachings of Mumberg et al, teaching use of the CYC1 promoter for expression in yeast because Mumberg et al teach that the CYC1

promoter can be altered to make a weak promoter for a lower level of expression, which can be desirable if low levels of a gene need to be expressed, for example, a toxic gene. It would have been obvious to one of ordinary skill in the art to use CYC1 because Mumberg et al teach that CYC1 is a constitutive promoter, which is desirable if one skilled in the art does not want to induce expression. In other words, the promoter can be regulated for low or high levels of expression. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 63, 75 and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stagljar et al, US 2005/0277116 and US 6,251,676 as applied to claims 48-55, 57-62, 64-67 above, and further in view of Ecker et al.

Applicants claims use of a promoter that confers low level expression, wherein the promoter is CUP1.

Stagljar et al, US 2005/0277116 and US 6,251,676 teaches all of the limitations as described above. They teach use of the CUP1 promoter in the pRS314(Nubl-ALG5) vector, however, they do not teach the CUP1 promoter in the bait vector.

Ecker et al (J. Biochem. 262(8): 3524-2527, 1987, especially p. 3524-2525) teach use of the CUP1 promoter for expression of the ubiquitin gene in yeast.

The ordinary skilled artisan, desiring to use a CUP1 promoter, would have been motivated to combine the teachings of Stagjlar et al, US 2005/0277116 and US

6,251,676, as described above, with the teachings of Ecker et al, teaching use of the CUP1 promoter for expression of the ubiquitin gene in yeast because Ecker et al teach that the CUP1 promoter can be partially repressed, which would lead to lower levels of expression. It would have been obvious to one of ordinary skill in the art to use CUP1 because Ecker et al teach that the important point is that the CUP1 promoter can be induced by copper, and if desired, high levels of expression can be attained. In other words, the promoter can be regulated for low or high levels of expression. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 71-73 and 78-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stagljar et al, US 2005/0277116 and US 6,251,676 as applied to claims 48-55, 57-62, 64-67 above, and further in view of Clarke et al. New claims 78-81 are added to the rejection.

Applicants claims use of low copy vector, wherein the vector has a CEN/ARS origin of replication.

Stagljar et al, US 2005/0277116 and US 6,251,676 teach all of the limitations as described above. They teach use of the CEN/ARS origin of replication in the NubI-ALG5 vector, however, they do not teach the CEN/ARS origin of replication in the bait vector.

Clarke et al (Ann. Rev. Genet. 19:29-56, 1985, especially pp. 32-33) teach use of the CEN/ARS vector as a low copy vector.

The ordinary skilled artisan, desiring to use a CEN/ARS vector, would have been motivated to combine the teachings of Stagjlar et al t, US 2005/0277116 and US 6,251,676, as described above, with the teachings of Clarke et al, teaching use of the CEN/ARS vector because Clarke et al teach that the copy number of a CEN/ARS vector is only 1-2 copies per cell. It would have been obvious to one of ordinary skill in the art to use a CEN/ARS vector because Clarke et al teach that the CEN/ARS vector greatly increases mitotic stability. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Response to Arguments Concerning Claim Rejections – 35 USC § 103(a)

Applicants have presented the following arguments which have not been found persuasive. The office stated that the Clarke teaches the CEN/ARS vector as a low copy vector. There is no rationale as to why one skilled in the art would desire this. Furthermore, CEN/ARS plasmids are less stable than normal yeast chromosomes.

These arguments are not found persuasive for the following reasons. Stagljar teaches plasmids with a CEN/ARS. Just because they did not use it in all of their plasmids, does not mean it is not an obvious choice. Low expression of genes can be desirable in many situations, for example to aid in stability. Plasmids are generally less stable than

chromosomes, and one of skill in the art would know that. However, Clarke also teaches that CEN/ARS plasmids greatly increase mitotic stability. Having any vector integrate creates more stability, whether it is a bait or prey vector.

Allowable Subject Matter

Claim 74 is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike whose telephone number is (571)272-5915. The examiner can normally be reached on M-F, 10:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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